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# Peripheral Activation of Formyl Peptide Receptor 2/ALX by Electroacupuncture Alleviates Inflammatory Pain by Increasing Interleukin-10 Levels and Catalase Activity in Mice

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## Abstract

In the context of the electroacupuncture (EA) neurobiological mechanisms, we have previously demonstrated the involvement of formyl peptide receptor 2 (FPR2/ALX) in the antihyperalgesic effect of EA. The present study investigated the involvement of peripheral FPR2/ALX in the antihyperalgesic effect of EA on inflammatory

cytokines levels, oxidative stress markers and antioxidant enzymes in an animal model of persistent inflammatory pain. Male Swiss mice underwent intraplantar (i.pl.) injection with complete Freund's adjuvant (CFA). Mechanical hyperalgesia was assessed with von Frey monofilaments. Animals were treated with EA (2/10 Hz, ST36-SP6, 20 minutes) for 4 consecutive days. From the first to the fourth day after CFA injection, animals received i.pl. WRW4 (FPR2/ALX antagonist) or saline before EA. Levels of inflammatory cytokines (TNF, IL-6, IL-4 and IL-10), antioxidant enzymes (catalase and superoxide dismutase), oxidative stress markers (TBARS, protein carbonyl, nitrite/nitrate ratio), and myeloperoxidase activity were measured in paw tissue samples. As previously demonstrated, i.pl. injection of the FPR2/ALX antagonist prevented the antihyperalgesic effect induced by EA. Furthermore, animals treated with EA showed higher levels of IL-10 and catalase activity in the inflamed paw, and these effects were prevented by the antagonist WRW4. EA did not change levels of TNF and IL-6, SOD and MPO activity, and oxidative stress markers. Our work demonstrates that the antihyperalgesic effect of EA on CFA-induced inflammatory pain could be partially associated with higher IL-10 levels and catalase activity, and that these effects may be dependent, at least in part, on the activation of peripheral FPR2/ALX.

**Keywords:** acupuncture; inflammation; pain; pro-resolving.

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